



## **Committee for Orphan Medicinal Products**

### **Public summary of positive opinion for orphan designation of recombinant human C1-inhibitor for the prevention of delayed graft function in organ transplant**

On 20 February 2007, orphan designation (EU/3/07/435) was granted by the European Commission to Pharming Group N.V., Netherlands, for recombinant human C1-inhibitor for the prevention of delayed graft function in organ transplant.

#### **What is delayed graft function in organ transplant?**

Delayed graft function occurs when, in the immediate stage after transplantation, the organ or the tissue transplanted from a donor to recipient does not start functioning properly. The cause of delayed graft function may be related to events occurring after the restoration of blood flow to a transplanted organ, which takes place after the temporary interruption of blood supply between removal of the organ from the donor and its placement in the receiving patient. This damage, called “reperfusion injury”, is associated with an inflammatory reaction, characterised by an invasion of white blood cell in the transplanted organ, and activation of a group of proteins called the complement system. Delayed graft function is life-threatening, due to the risk of graft loss.

#### **What is the estimated number of patients at risk of developing the condition?**

At the time of designation, the number of patients at risk of delayed graft function in organ transplant was estimated to be approximately 0.5 people in 10,000 per year in the European Union (EU)\*. This is equivalent to a total of around 23,000 people per year, which is below the threshold for orphan designation, which is 5 people in 10,000. This is based on the information provided by the sponsor and knowledge of the Committee for Orphan Medicinal Products (COMP).

#### **What methods of prevention are available?**

At the time of submission of application for orphan drug designation, there was no method authorised in the European Union for the prevention of delayed graft function after solid organ transplant. The preventive measures to reduce delayed graft function in organ transplant consist of donor management and organ preservation solutions.

#### **How is this medicine expected to work?**

Recombinant human C1-inhibitor is analogous to a natural human protein, C1-inhibitor, which circulates in low levels in the blood. C1-inhibitor works by blocking the activation of the complement system; complement activation is thought to play a critical role in the reperfusion injury. Blocking complement activation is known to improve the function of transplanted kidneys in experimental models.

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\*Disclaimer: For the purpose of the designation, the number of patients affected by the condition is estimated and assessed on the basis of data from the European Union (EU 25), Norway, Iceland and Liechtenstein. This represents a population of 459,700,000 (Eurostat 2004).

**What is the stage of development of this medicine?**

At the time of submission of the application for orphan designation, no clinical trials with recombinant human C1-inhibitor in patients with delayed graft function in organ transplant were initiated.

Recombinant human C1-inhibitor was not authorised anywhere worldwide for prevention of delayed graft function in organ transplant, at the time of submission. Orphan designation of recombinant human C1-inhibitor was granted in the United States for the condition in June 2006.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 10 January 2007 a positive opinion recommending the grant of the above-mentioned designation.

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Opinions on orphan medicinal product designations are based on the following three criteria:

- the seriousness of the condition;
- the existence of alternative methods of diagnosis, prevention or treatment;
- either the rarity of the condition (affecting not more than 5 in 10,000 people in the Community) or insufficient returns on investment.

Designated orphan medicinal products are products that are still under investigation and are considered for orphan designation on the basis of potential activity. An orphan designation is not a marketing authorisation. As a consequence, demonstration of quality, safety and efficacy is necessary before a product can be granted a marketing authorisation.

**For more information:**

Sponsor's contact details:

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**Translations of the active ingredient and indication in all EU languages  
and Norwegian and Icelandic**

<b>Language</b>	<b>Active Ingredient</b>	<b>Indication</b>
English	Recombinant human C1-inhibitor	Prevention of delayed graft function after solid organ transplantation
Bulgarian	Рекомбинантен човешки C1 – инхибитор	Предотвратяване на забавено функциониране на присадката при органна трансплантация
Czech	Rekombinantní lidský inhibitor složky komplementu C1	prevence opožděné funkce štěpu po transplantaci orgánu
Danish	Rekombinant human C1-inhibitor	Forebyggelse af forsinket transplanteringsfunktion i forbindelse med organtransplantation
Dutch	Recombinant humaan C1-remmer	Preventie van vertraagde orgaan transplantaatfunctie
Estonian	Inimese rekombinantne C1-inhibiitor	Transplantaadi funktsiooni hilinemise tõkestamine pärast elundisiirdamist
Finnish	Rekombinantti ihmisen C1-inhibiittori	Siirännäisen toimintaviiveen ehkäisy elinsiirrossa
French	Inhibiteur C1 humain recombinant	Prévention des retards fonctionnels du greffon dans la greffe d'organe.
German	Rekombinanter humaner C1-Inhibitor	Vorbeugung der verzögerten Transplantatfunktion nach Organtransplantation
Greek	Ανασυνδυασμένος ανθρώπινος αναστολέας C1	Πρόληψη της αργοπορημένης λειτουργίας του μοσχεύματος κατά τη μεταμόσχευση οργάνων
Hungarian	Rekombináns humán C1-inhibitor	Szervtranszplantációt követő késői graftfunkció megelőzése
Italian	C1-inibitore umano ricombinante	Prevenzione del ritardo nella funzionalità nell'organo trapiantato
Latvian	Rekombinants cilvēka C1 inhibitors	Aizkavētas transplantāta funkcijas profilaksei pēc parenhimatozo orgānu transplantācijas
Lithuanian	Rekombinantinis C1 žmogaus inhibitorius	Vėlyvos transplantato atmetimo reakcijos prevencija po organo transplantavimo
Polish	Rekombinowany ludzki inhibitor C1	Zapobieganie opóźnieniu podjęcia czynności przez przeszczepiony narząd
Portuguese	Inibidor C1- humano recombinante	Prevenção do atraso funcional do órgão transplantado
Romanian	Inhibitor C1 uman recombinant	Prevenirea întârzierii funcționării grefei de organ transplantat
Slovak	Rekombinantný humánný C1 inhibítor	Prevenia oneskorenej funkcie štepu po transplantácii orgánu
Slovenian	Rekombinantni humani inhibitor C1	Preprečevanje zapoznelega začetka delovanja presadka po presaditvi organa
Spanish	Inhibidor C1 humano recombinante	Prevenición del retraso de la función del órgano transplantado
Swedish	Rekombinant human C1-inhibitor	Förebyggande av fördröjd transplantatfunktion i samband med organtransplantation
Norwegian	Rekombinant human C1-inhibitor	Forebyggelse av forsinket transplantatfunksjon i forbindelse med organtransplantasjon
Icelandic	Raðbrigða manna C1 hemill	Til að koma í veg fyrir síðkomna starfsbilun eftir líffæraígræðslu